UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,197	04/12/2004	David C. Crossman	24299-514 CIP2A DIV	4039

30623 7590 12/20/2007

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY
AND POPEO, P.C.
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER	
MYERS, CARLA J	
ART UNIT	**PAPER NUMBER**
1634	

MAIL DATE	DELIVERY MODE
12/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,197	CROSSMAN ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-15 and 80-83* is/are pending in the application.

4a) Of the above claim(s) *80-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the amendment filed July 19, 2007. Applicant's arguments have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. This action is made final.

In particular, the rejection of claims 8-15 under 35 U.S.C. 102(b) as being anticipated by the Cominelli et al (WO 97/25445; July 1997) is withdrawn in view of the amendments to the claims. As discussed below, the claims as amended are entitled to the filing date of March 10, 1997, and thereby Cominelli is not prior art to the presently claimed invention. Similarly, the rejections over Duff et al (PGPUB 20050064453), Duff et al (U.S. Patent No. 6730476), Duff et al (U.S. Patent No. 6268142), Duff et al (U.S. Patent No. 5,698,399), Duff et al (U.S. Patent No. 6713253), Francis (PGPUB 20060252055), Duff et al (U.S. Patent No. 6706478), and Duff (PGPUB 20040152124) are withdrawn in view of the amendment to the claims.

Further, the previous provisional rejection of claims 8-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of copending U.S. Application No. 10/838,503 has been obviated by the amendments to the claims of '503. The provisional rejection of claims 8-10 and 12-15 d under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 15-20 of copending U.S. Application No. 10/914,396 is withdrawn in view of the amendment to the present claims to omit the recitation of a

primer that hybridizes 5' or 3' to an allele in linkage disequilibrium with the IL-1RN VNTR allele 1.

Election/Restrictions

2. In the reply of October 26, 2006, Applicant elected Group IV, directed to kits comprising primers that hybridize to IL-1RN (VNTR) allele 1, and the particular primer of SEQ ID NO: 7. Accordingly, the non-elected subject matter of the primer of SEQ ID NO: 8 (claim 11) and claims 80-83 drawn to kits comprising the additional primers that hybridize to alternative IL-1RN, IL-1A and IL-1B alleles are withdrawn from consideration as being drawn to a non-elected invention.

Terminal Disclaimer

3. The terminal disclaimers filed on July 19, 2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 6,268,142 and 6,746,839 have been reviewed and are accepted. The terminal disclaimers have been recorded.

Priority

4. The claims have been amended to delete the recitation that the kits are for determining the existence of susceptibility to developing restenosis in a subject. Accordingly, the claimed subject matter is entitled to priority to applications 09/578,534, 09/431,352, 09/320,395 and 08/813,456 because these applications disclose kits comprising a primer that hybridizes 5' or 3' to an IL-1RN (VNTR) allele and particularly disclose the primer of SEQ ID NO: 7. Note that in applications '352, '395 and '456, present SEQ ID NO: 7 is referred to therein as SEQ ID NO: 1.

Maintained Rejections

Claim Rejections - 35 USC § 112 - Written Description

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-10 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

The following rejection was originally set forth in the Office action of January 19, 2007 and has been modified to address the amendments to the claims.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved

by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the claims are drawn broadly to encompass kits comprising a first primer that hybridizes 5' or 3' to an IL-RN (VNTR) allele 1. The claims do not define the primers in terms of any particular structural features, such as the coding or noncoding sequence to which the primers hybridize, the location within the coding or noncoding region to which the primers hybridize etc.

The specification (Figure 3; SEQ ID NO: 17) teaches the nucleotide sequence of the IL-1RN gene. The specification (page 66-67) further teaches that the IL-1RN (VNTR) allele 2 is associated with a lower restenosis rate in patients with SVD. The specification (page 11) also discloses primers consisting of SEQ ID NO: 7 and 8 and the use of these primers to amplify sequences comprising the IL-RN (VNTR) allele. Accordingly, the specification provides adequate written description for kits comprising a primer that hybridizes to IL-1RN (SEQ ID NO: 17) 5' or 3' to IL-1RN (VNTR) allele 1, particularly wherein said primer is SEQ ID NO: 7.

It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. restriction map,

biological activity of an encoded protein product, etc.). In the instant case, no such identifying characteristics have been provided for coding or non-coding sequences 5' or 3' to the IL-1RN gene.

However, the claims as written are inclusive of a potentially large genus of alleles. The claims do not define the primers in terms of any particular structural features, since the primers may hybridize to any sequence (i.e., any gene or noncoding region) that is 5' or 3' of the IL-1RN (VNTR) allele 1. Yet, the coding and non-coding sequences of genes that are 5' and 3' of the IL-1A gene have not been described in the specification.

While the sequence of the IL-1RN gene was known in the art at the time the invention was made, this disclosure does not allow the skilled artisan to envision all of the contemplated primers which may hybridize 5' or 3' to this gene. The information provided regarding the IL-1RN (VNTR) allele does not constitute an adequate written description of the broadly claimed subject matter, such that one of skill in the art could readily envision the detailed chemical structure of the nucleic acids encompassed by the claims. Adequate written description requires more than a mere statement that such nucleic acids are part of the invention and reference to a potential method for identification. The particular nucleic acids are required.

Thereby, the disclosure in the specification of two primers (SEQ ID NO: 7 and 8) which hybridize 5' and 3' to the IL-1RN (VNTR) allele is not considered to constitute a representative number of primers that may hybridize to any coding or non-coding sequence 5' or 3' of the IL-1RN (VNTR) allele. For these reasons, Applicants have not

provided sufficient evidence that they were in possession, at the time of filing, of the invention as it is broadly claimed and thus the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Response to Remarks:

In the response, Applicants traverse this rejection by stating that one of ordinary skill in the art could make additional primers to detect IL-1RN VNTR allele 1 based on the physical properties of the primers that are provided – i.e., their ability to make an amplification product that can be used to detect IL-1RN VNTR alleles. However, the present claims are not limited to primers which are used to generate an amplification product that can detect an IL-1RN VNTR allele. Rather, the present claims require only a primer that is defined functionally by the fact that it hybridizes 5' or 3' to allele 1 of IL-1N VNTR.

Applicants assert that they have provided the sequence of IL-1RN and have disclosed the sizes of amplification products produced using SEQ ID NO: 7 and 8. This argument has also been fully considered but is not persuasive because the claims are not limited to primers consisting of SEQ ID NO: 7 or 8, nor are the claims limited to primers that hybridize to sequences of the IL-1RN gene of SEQ ID NO: 17. Rather, the claims include any primer that hybridizes to any coding or non-coding sequence that are

5' or 3' of IL-1RN VNTR (i.e., sequences upstream and downstream of the IL-1RN gene).

Applicants further cite the art of Breslauer, Rychlik and (1989) and Rychlik (1990) as teaching methods for designing PCR primers. It is argued that knowledge in the art of how to design primers "allows those having ordinary skill in the art to not only select and/or design primers for just about any given DNA sequence, but to optimize the amount of specific product produced by these primers." These arguments and the cited art have been fully considered but are not persuasive. Again, it is emphasized that the claims are not limited to primers that hybridize to IL-1RN gene sequences. Rather, the claims are drawn to primers that may hybridize to any coding or non-coding sequences that are 5' or 3' of the IL-1RN gene. The coding and non-coding sequences that flank the IL-1RN gene are not disclosed in the specification and the specification does not exemplify a single primer within the broadly claimed genus encompassed by the claims of primers which hybridize to any coding or non-coding sequences that are 5' or 3' of the IL-1RN gene. Further, while methods are well known in the art as to how to design primers to known nucleic acids sequences, possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. See University of Rochester, 358 F.3d at 927, 69 USPQ2d at 1895.

This finding is also emphasized in *Ex Parte Kubin* (No. 2007-0819, Bd. Pat. App. & Int. May 31, 2007), wherein it is stated that :

"Although there is often significant overlap" between the enablement and written description requirements, "they are nonetheless independent of each other." University of Rochester, 358 F.3d at 921, 69 USPQ2d at 1891. An "invention may be enabled even though it has not been described." Id. Such is the situation here. While we conclude one skilled in the art would have been able to make and use the full scope of claim 73 through routine experimentation, we find Appellants did not describe the invention of claim 73 sufficiently to show they had possession of the claimed genus of nucleic acids. See, e.g., Noelle v. Lederman, 355 F.3d 1343, 1348, 69 USPQ2d 1508, 1513 (Fed. Cir. 2004) ("invention is, for purposes of the 'written description' inquiry, whatever is now claimed"). Accordingly, a showing of how to potentially identify and make other primers that hybridize 5' or 3' of IL-1RN VNTR allele 1 is not sufficient to establish that Applicant's were in possession of the invention as broadly claimed of a genus of primers that hybridize to any coding or non-coding sequence 5' or 3' of the IL-1RN gene.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-10 and 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by the GIBCO BRL Catalog (1995/1996; pages 18-15 to 18-16).

The GIBCO BRL Catalog discloses a kit for labeling DNA wherein the kit comprises: a) a random primer solution (i.e., primers which hybridize 3' and 5' to the

.IL-1RN allele 1; b) biotin-14-dCTP (i.e., a detection means for performing a sequencing or primer extension specific method or an amplification means); c) dNTPs and DNA polymerase (i.e., a detection means for performing a sequencing or primer extension specific method or an amplification means); and d) a control DNA. It is a property of the primers present in the random primer solution that the primers hybridize to sequences in a range of about 25 to 2500 base pairs. Accordingly, the GIBCO BRL kit anticipates the claimed invention.

Response to Remarks:

In the response, applicants state that GIBCO does not teach a kit comprising primer oligonucleotides that hybridize 5' or 3' to IL-1RN VNTR allele 1.

This argument has been fully considered but is not persuasive. GIBCO BRL teaches a random primer solution. The random primers have the ability to hybridize to any nucleic acid sequence. Accordingly, it is a property of the primers that they hybridize 5' or 3' of IL-1RN VNTR allele 1 since the primers are capable of hybridizing to any nucleic acid. The present claims do not require that the primer hybridizes with any specificity or under any particular hybridization conditions. Further, the claimed primers are not defined in terms of a particular nucleotide sequence or a particular length. Accordingly, the kits of GIBCO BRL comprising a random primer solution anticipates the claimed invention.

New Grounds of Rejection

7. Claims 8-11 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Mansfield et al (Gastroenterology. 1994. 196: 637-642).

Mansfield (Table 2) teaches a primer consisting of the sequence 5'-CTCAGCAACACTCCTAT-3', wherein the primer is identical to present SEQ ID NO: 7. Mansfield further teaches a composition comprising this primer together with a second primer consisting of the sequence of 5'-TCCTGGTCTGCAGGTAA (i.e., present SEQ ID NO: 8). The primer pair is characterized as hybridizing 5' and 3', respectively, to the IL-1RA (i.e., IL-1RN) VNTR allele 1 (see Table 2). The primers hybridize to sequences of the IL-1RN gene at a distance between 25 to 2500 bp apart because the primers amplify IL-RN sequences to obtain PCR products of 410 bp (allele 1), 240 bp (allele 2) and 500 bp (allele 3). Thus, the primer pair is used in a primer specific extension reaction.

It is noted that in the absence of any recitation in the claims or any direction in the specification to the contrary, the recitation in the claims of a "kit" reads on component parts capable of being assembled or a plurality of elements grouped together as a kit. Accordingly, the word "kit" does not impart any additional special structural or functional features which distinguishes the claimed kit over the isolated nucleic acids of Mansfield. Since the primers of Mansfield have the property of hybridizing 5' and 3' to allele 1 of IL-1RN VNTR and the first primer of Mansfield consists of the sequence of present SEQ ID NO: 7, the primers of Mansfield anticipate the claimed invention.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mansfield in view of Erlich (U.S. Patent No. 5,468,613).

The teachings of Mansfield are presented above.

Regarding claims 8-11 and 13, to the extent that the term "kit" is intended to refer to a structural container, Mansfield does not teach packaging the IL-1RN/IL-1RA PCR primers into such a container. Regarding claims 12, 14 and 15, Mansfield does not teach packaging the IL-1RN/IL-1RA PCR primers together with a detection means, amplification means and a control into a kit and does not teach labeling primers.

However, Erlich teaches the concept of generating kits for performing nucleic acid amplification reactions, wherein the kits comprise PCR primers, amplification means, detection means and a control nucleic acid (see col. 18). In view of the disclosure of Erlich, it would have been obvious to one of ordinary skill in the art at the

time the invention was made to have packaged the Il-1RN/IL-1RA primers of Mansfield into a kit, along with the other reaction components required to perform PCR, including amplification reagents, detection means and control nucleic acids in order to have achieved the expected benefits of convenience and cost-effectiveness for practioners wishing to amplify IL-1RN nucleic acids, and detect the presence of the IL-1RN VNTR polymorphism.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Carla Myers/

Primary Examiner, Art Unit 1634